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Accuracy of Radionuclide Ventriculography for Estimation of Left Ventricular Volume Changes and End-Systolic Pressure-Volume Relations

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Estimation of left ventricular end-systolic pressure-volume relations depends on the accurate measurement of small changes in ventricular volume. To study the accuracy of radionuclide ventriculography, paired radionuclide and contrast ventriculograms were obtained in seven dogs during a control period and when blood pressure was increased in increments of 30 mm Hg by phenylephrine infusion. The heart rate was held constant by atropine infusion.

The correlation between radionuclide and contrast ventriculography was excellent. In the individual animals, the average r value for left ventricular volume was 0.96 ± 0.03 (± SD) ($p = 0.001$, $n = 7$) and the mean r value for end-systolic volume changes was 0.90 ± 0.08 ($n = 7$, range 0.76 to 0.99). For the entire series, there were 33 end-systolic volume changes, and there was an equally strong radionuclide-contrast correlation ($r = 0.89$, $p < 0.001$, $n = 33$), even though the volume changes averaged only 11.9 ± 8.2 ml (range 0.3 to 38.1).

The systolic pressure-volume relations were linear for both radionuclide and contrast ventriculography ($r = 0.98$ and 0.97, respectively, $n = 7$). The mean slope for radionuclide ventriculography (2.9 ± 1.4) was lower than the mean slope for contrast ventriculography (4.8 ± 1.7) ($p = 0.004$); however, the slopes correlated well ($r = 0.81$, $n = 7$, $p = 0.026$).

The radionuclide-contrast volume relation was compared using background subtraction, attenuation correction, neither of these or both. By each method, radionuclide ventriculography was valid for measuring small changes in left ventricular volume and for defining end-systolic pressure-volume relations.

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The left ventricular end-systolic pressure-volume relation is an index of myocardial contractility that is affected only slightly by ventricular preload or heart rate (1). Recently, studies have been extended from the isolated heart (2,3) to intact animals (4–6) and to humans (7–15).

Estimation of left ventricular end-systolic pressure-volume relations depends on the measurement of small changes in left ventricular end-systolic volume and accurate determination of the arterial pressure. Radionuclide ventriculography can quantitate absolute left ventricular volume (16–21) and cardiac output (22–24); however, there has been no direct validation of the radionuclide method for measuring small end-systolic volume changes and little validation of radionuclide ventriculography for estimating pressure-volume relations. Thus, this study was designed to compare left ventricular volume changes determined by radionuclide-ventriculography with volume changes on near simultaneous contrast ventriculography. We also compared pressure-volume relations by the contrast and radionuclide methods. The

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intrathoracic attenuation of radioactivity was measured to aid the radionuclide calculations.

Methods

Experimental preparation. Seven mongrel dogs, both male and female, were studied. Their weights ranged from 17 to 25 kg (average 21.4). They were sedated with intramuscular morphine sulfate and intravenous diazepam, secured in a supine position and ventilated (Harvard Apparatus) using endotracheal intubation. A plastic cannula was placed in a peripheral vein, and a sheath was placed in the right femoral vein. A 7F pigtail catheter was advanced to the thoracic aorta percutaneously by way of the left femoral artery.

Attenuation measurement. Technetium-99m (40 to 50 mCi [average 48.3] in 1 ml) was injected into a balloon-tipped catheter that was placed on the surface of the chest and imaged in the left anterior oblique position. Then the balloon was aspirated and the catheter was advanced through the femoral vein to the right atrial-inferior vena cava junction. The technetium-99m was reinjected into the balloon, and another image of the catheter tip was obtained, maintaining the same angle of view and camera-computer characteristics.

The attenuation factor (AF) was calculated as follows:

$$AF = \frac{\text{Counts/s outside thorax}}{\text{Counts/s inside thorax}}.$$

The data were corrected for camera-computer deadtime losses which were determined by collecting images of incremental amounts of technetium-99m. In separate tests on three catheters, there was an internal "loss" of only 1.2% (range 0.4 to 1.4) of the radioactivity by the process of injection, aspiration and reinjection.

Study protocol. The intraarterial pressure and an electrocardiographic rhythm strip were recorded continuously on paper using an Electronics for Medicine recorder (model VR-12). Atropine sulfate was administered continuously through the femoral vein using an infusion pump (Harvard Apparatus) to maintain a constant heart rate.

Red blood cells were labeled in vivo (25). After the attenuation measurements, the technetium-99m pertechnetate was aspirated from the catheter and injected intravenously. After isotope distribution, electrocardiographic R wave-gated cardiac blood pool images were obtained in the left anterior oblique projection, recording the 140 keV energy peak, with a 15% window, employing a gamma camera (Picker DynaCamera 4) equipped with a medium resolution parallel-hole collimator. They were stored as gated 5 minute, 20 frame studies at 30 to 40 ms/frame in a 64 × 64 image matrix using a PDP 11/05 computer (Digital Equipment Corporation) equipped with variable hardware zoom. The aortic root pressure was recorded continuously. At the end of imaging, 10 ml of arterial blood was withdrawn and saved for subsequent left ventricular volume calculations. The dog was then positioned for contrast ventriculography by moving the imaging table. The aortic root pressure was measured and the catheter was advanced to the left ventricle. The ventilator was stopped and 25 ml of a mixture of meglumine and sodium diatrizoate (Renografin-76, E.R. Squibb) was injected at 12 ml/s, recording the ventriculogram on 35 mm film at 60 frames/s.

After this initial pair of measurements, the arterial blood pressure was increased in increments of 20 to 40 mm Hg by continuous infusion of phenylephrine hydrochloride (0.1 μg/ml) and was held stable at the new level. Repeat paired radionuclide and contrast ventriculograms were obtained at two or three increments of systolic pressure.

The blood samples were pipetted into petri dishes (Oxford pipette, model CR-17739) (0.5% error full scale) and were counted on the face of the collimator for 5 minutes using the same imaging system.

Data analysis. The contrast ventriculograms were traced manually. The left ventricle was outlined in the frames with the largest volume (defined as end-diastole) and smallest volume (end ejection) defined as end-systole. The first well opacified cycle was used, excluding ectopic and postectopic beats. The volumes were calculated by the area-length method for single plane studies with correction for magnification (26). Mitral regurgitation was not observed.

The radionuclide volumes were estimated using semiautomated software for border definition and a variable region of interest technique (27). The end-diastolic and end-systolic frames were identified based on the greatest and least radioactivity during the cardiac cycle. End-diastolic volume (EDV) was calculated according to methods proposed by Slutsky et al. (16,28) and Dehmer et al. (29) with correction for radioactive decay. The end-systolic volume (ESV) was calculated as ESV = EDV (1 − EF), where EF = ejection fraction. The correlation coefficient between radionuclide and contrast ventriculography for the ejection fraction is 0.93 (27) and for left ventricular volume is 0.93 (30).

The radionuclide and contrast ventriculograms were analyzed independently, in duplicate, by a separate observer for each. The duplicate results were averaged. The radionuclide volume units were calculated by using four methods: the uncorrected "raw" results, background subtraction alone, attenuation correction alone and the combination of background subtraction and attenuation correction. Each set of results was compared with the contrast ventricular volume.

The systolic volume changes were calculated as the differences in end-systolic volume between ventriculograms obtained before and after pressure afterload for both the radionuclide and contrast studies. Diastolic volume changes

were calculated similarly. In the text and figures the correlation of radionuclide and contrast volume and volume changes is shown using background subtraction for the radionuclide results.

The aortic pressure was measured once a minute during radionuclide imaging. The systolic, diastolic and end-systolic pressures were averaged. The aortic pressure preceding contrast ventriculography was used for calculating the contrast pressure-volume relations.

The radionuclide volume units were converted to volume (in milliliters) by a regression equation derived from the group data relating the radionuclide volume units to the contrast volume estimates. The end-systolic pressures and volumes were tabulated and graphed. The linearity and slope of the pressure-volume relation and the ventricular volume extrapolated to zero pressure (V_0) were determined by linear regression analysis. For the radionuclide method, the pressure-volume relations were examined with ventricular volume estimated using three methods: background subtraction, attenuation correction and the combination of these. The background-corrected data are employed in the Results section.

Data were analyzed using a computer data base management system (CLINFO, supplied by the Division of Research Resources, National Institutes of Health, Bethesda, Maryland) employing linear regression and paired *t* tests as appropriate. Statistical significance was defined as probability (p) < 0.05.

Results

There were 25 pairs of radionuclide and contrast ventriculograms. Dogs 1 to 3 had three paired studies; Dogs 4 to 7 had four paired studies. The end-systolic pressure for the control and pressure afterload studies averaged 123 ± 24 (± SD), 149 ± 29, 183 ± 24 (n = 7) and 210 ± 7 mm Hg (n = 4 for the latter). Pressure values were nearly identical on paired radionuclide and contrast studies (mean difference 1.4 mm Hg, n = 25, p = NS). The heart rate

Table 1. Left Ventricular Pressure, Volume and Radioactivity

Dog	VGRAM	ESP	CVGED	CVGES	RVGED	RVGES	Atten
1	1	115	72.0	25.4	28.6	12.0	2.2
	2	137	70.2	31.4	27.2	12.5	
	3	176	83.5	46.1	33.1	19.6	
2	1	146	55.7	16.1	13.4	3.5	1.6
	2	177	53.5	23.2	18.2	5.6	
	3	208	48.5	25.4	17.9	7.3	
3	1	159	93.4	38.0	20.8	6.8	2.2
	2	189	98.1	44.7	23.2	9.7	
	3	216	100.6	46.3	24.7	11.5	
4	1	95	47.9	16.5	10.5	4.4	2.6
	2	128	55.3	22.4	15.0	7.2	
	3	183	60.0	33.3	17.9	10.2	
	4	204	63.3	35.8	20.5	13.1	
5	1	120	55.6	21.9	14.4	6.9	2.4
	2	142	67.6	32.5	18.7	9.4	
	3	167	84.8	46.2	22.6	14.0	
	4	218	109.5	60.0	27.2	18.5	
6	1	124	87.1	38.5	10.8	3.9	2.9
	2	166	94.3	47.8	14.1	5.2	
	3	185	100.6	48.1	18.7	8.0	
	4	213	109.5	60.0	22.9	12.1	
7	1	98	72.4	24.5	14.9	5.4	2.1
	2	106	74.1	29.2	18.4	6.9	
	3	144	64.9	31.6	18.6	7.6	
	4	205	71.3	41.4	15.5	9.9	

Atten = radioactivity attenuation factor; CVGED and CVGES = contrast ventriculographic end-diastolic and end-systolic volume, respectively; ESP = end-systolic pressure; RVGED and RVGES = radionuclide ventriculographic end-diastolic and end-systolic volume units, respectively (using background subtraction); VGRAM = number of ventriculogram. See text for details.

averaged 107 ± 7.2 beats/min for the radionuclide study and 105 ± 8.1 beats/min for the contrast study (p = NS). The contrast left ventricular volumes ranged from 48 to 110 ml at end-diastole and from 16 to 60 ml at end-systole. The radionuclide volume units ranged from 10.5 to 33.1 at end-diastole and from 3.5 to 19.6 at end-systole (Table 1).

Reproducibility. The reproducibility for contrast volume determinations was excellent. The intraobserver difference for 23 duplicate tracings was 1.0 ± 0.9 ml at end-diastole with a correlation coefficient (r) of 0.998 ($p < 0.001$). For end-systole, the difference was 1.4 ± 0.9 ml (r = 0.99). These were 1.3 and 3.9% of the average left ventricular volume at end-diastole and end-systole, respectively. The interobserver difference for 11 duplicate studies at end-diastole was 6.1 ± 4.6 ml (r = 0.98). At end-systole, the interobserver difference was 3.6 ± 3.6 ml (r = 0.95). These differences were 8.1 and 10.2% of the average end-diastolic and end-systolic volumes, respectively.

The radionuclide reproducibility was also excellent. The intraobserver difference for 22 duplicate determinations (before correction to "true" volume by a regression equation) was 0.5 ± 0.4 volume units at end-diastole with a close correlation (r = 0.99, $p < 0.001$). For end-systole, the difference was 0.4 ± 0.3 units (r = 0.99). These were equivalent to 3.3 and 5.6% of the average left ventricular volumes at end-diastole and end-systole, respectively. The interobserver difference for 16 duplicate studies was 2.8 ± 2.1 units for end-diastole (r = 0.92). At end-systole, the difference was 1.9 ± 1.5 units (r = 0.96). These differences were 14.4 and 9.2% of the average end-diastolic and end-systolic volumes, respectively.

Volume correlation. The relation between left ventricular volumes determined by contrast and radionuclide ventriculography was close for the individual animals. Table 1 lists the ventricular volumes estimated by both techniques, the radioactivity attenuation factors and the end-systolic arterial pressure. Figure 1 demonstrates the volume relation for a representative animal. The mean correlation for the seven dogs was 0.96 ± 0.03 (± SD). Table 2 shows the close correlations between radionuclide and contrast estimates of volume and for changes in volume in the individual animals.

For the group data, the relation for volume determined by radionuclide and contrast ventriculography was significant but much looser (Table 3), because of differences in the intrathoracic background radioactivity and attenuation. The influence of these factors on volumes calculated from radionuclide images was examined. The slope for the relation between radionuclide volume units and the contrast volume estimates was 0.41 using uncorrected radionuclide data. Background subtraction lowered the slope to 0.22. Attenuation factors averaged 2.3 ± 0.4. The combination of background subtraction and attenuation correction increased the slope to 0.46, but did not improve the volume correlation. The closest correlation between radionuclide and contrast volume estimates was produced by simply multiplying the measured left ventricular radioactivity by the individual attenuation factor (r = 0.87, slope = 1.06), excluding background subtraction. However, neither attenuation correction nor the combination of attenuation and background correction could improve the estimation of end-systolic volume change beyond simple background subtraction. Thus, that method was employed.

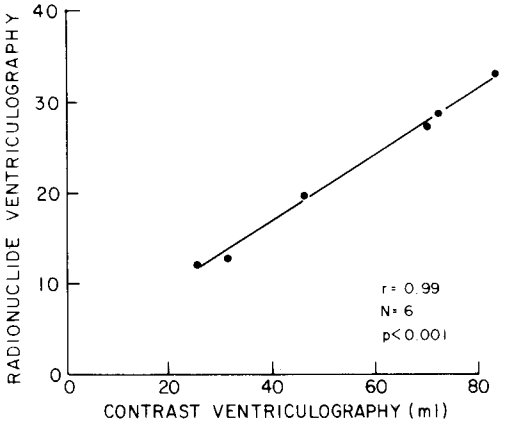


Figure 1. Relation between radionuclide (units) and contrast (ml) volume estimates in an individual animal (Dog 5). The correlation is strong.

End-systolic volume changes. The correlation between the radionuclide and contrast methods for defining changes in volume was examined for the individual dogs and for the entire group. For a dog with three pairs of ventriculograms, there were six possible combinations of volume differences: 2-1, 3-2 and 3-1, both for end-diastole and for end-systole, making a total of six. For a dog with four pairs of ventriculograms, there were 12 possible volume changes. Figure 2 demonstrates the results in the individual dogs with the smallest and the largest sets of contrast ventriculographic end-systolic volume changes. In Figure 2A, the smallest set of volume changes ranged from only 1.6 to 8.3 ml. Nevertheless, the radionuclide volume changes correlated well with the contrast volume changes (r = 0.91, p = 0.28, n = 3). The latter did not achieve statistical significance because of the limited data. In Figure 2B, the largest set of end-systolic volume changes ranged from 10.6 to 53.9 ml. The correlation coefficient between radionuclide and contrast volume changes was 0.99 ($p < 0.001$, n = 6).

For the entire group of seven dogs, there were 66 volume changes. On contrast ventriculography, the 33 end-systolic changes ranged from 0.3 to 38.1 ml (mean 11.9 ± 8.1). The 33 end-diastolic volume changes ranged from 1.1 to 53.9 ml (mean 9.5 ± 13.5). For the changes in end-systolic volume, the mean of the r values for the individual studies was 0.90 ± 0.08 (n = 7); in five of the seven studies, the r value was 0.88 to 0.99. Figure 3 shows the close corre-

Table 2. Radionuclide and Contrast Ventriculographic Correlations

	Left Ventricular Volume			Left Ventricular Volume Changes		
Dog	ED	ES	ED+ES	ED	ES	ED+ES
1	0.995	0.974	0.997	0.997	0.938	0.962
2	−0.697	0.970	0.929	0.128	0.837	−0.042
3	0.999	0.979	0.990	0.994	0.908	0.933
4	0.999	0.977	0.935	0.993	0.882	0.882
5	0.990	0.998	0.988	0.945	0.988	0.917
6	0.996	0.945	0.919	0.977	0.762	0.839
7	−0.388	0.996	0.953	−0.372	0.985	0.331
Mean	0.558	0.977	0.959	0.666	0.900	0.680
SD	0.797	0.018	0.033	0.558	0.081	0.585
SE	0.286	0.007	0.012	0.211	0.003	0.145

ED = end-diastolic; ES = end-systolic.

lation for the entire group of end-systolic volume changes ($r = 0.89$). For the combined end-diastolic and end-systolic data (Table 2), the calculated radionuclide volume changes were significantly related to the contrast changes ($r = 0.68$) by using background subtraction ($r = 0.79$ by the combination of background and attenuation correction). The correlation coefficient for end-diastolic volume changes was 0.67 by background subtraction (and was 0.54 by combined background and attenuation correction), but the reason for the apparent lower accuracy at end-diastole may be traced to the results of two dogs (Table 2, Dogs 2 and 7). In all other studies, the correlation between radionuclide and contrast methods for defining changes in end-diastolic volumes was 0.95 or greater.

End-systolic pressure-volume relations. The end-systolic pressure-volume relations were highly linear for both the contrast and the radionuclide methods (Fig. 4). The correlation coefficients were 0.94 or greater (average 0.97). The linearity was preserved whether peak, mean or end-systolic pressure was employed. The pressure-volume slopes were shallower by radionuclide than by contrast ventriculography, averaging 2.9 ± 1.4 mm Hg per unit volume for the radionuclide method and 4.8 ± 1.7 mm Hg/ml for the contrast method. The radionuclide slopes were lower ($p = 0.004$), but the correlation between slopes on radionuclide and contrast ventriculography was statistically significant ($r = 0.81$, $p = 0.026$, $n = 7$). The extrapolated point (V_0) averaged −34.8 ± 18.0 ml for the radionuclide results and −2.5 ± 13.9 ml for the contrast results; the difference was significant ($p = 0.004$).

Discussion

This study demonstrated the accuracy of radionuclide ventriculography for estimating changes in left ventricular volume. This is a key factor for studies of left ventricular end-systolic pressure-volume relations, because such small volume changes determine the slope of the relation once the pressure is known.

Reproducibility of contrast and radionuclide volume estimates. Both the intraobserver and interobserver results were highly reproducible. The intraobserver reproducibility was slightly better than the interobserver results, as might be expected.

Estimates of volume changes. For the individual dogs, nearly all the end-systolic volume changes on radionuclide ventriculography correlated well with changes on contrast ventriculography (Table 2). Estimates of end-diastolic volume changes demonstrated occasional discrepancies. The accuracy of the volume changes depended on the accuracy of each of the ventriculograms. The radionuclide volumes represented several hundred beats collected over 5 minutes. The contrast volumes were determined by analysis of a single beat. There is a tight concordance between the results

Table 3. Radionuclide Volume Regressions

Correction Factors	r	p Value	n	Equation (y = b + mx)	SEE
None	0.83	<0.001	50	RVG = 10.17 + 0.41 CVG	7.11
A	0.87	<0.001	50	RVG = 17.54 + 1.06 CVG	15.82
B	0.78	<0.001	50	RVG = 2.38 + 0.22 CVG	4.52
A+B	0.74	<0.001	50	RVG = 5.08 + 0.46 CVG	10.78

A = attenuation correction; B = background correction; CVG = contrast ventriculographic; RVG = radionuclide ventriculographic units; SEE = standard error of estimate. In linear regression equation, x = CVG, y = RVG units when x = 0 and m = slope of line describing the relation of x and y.

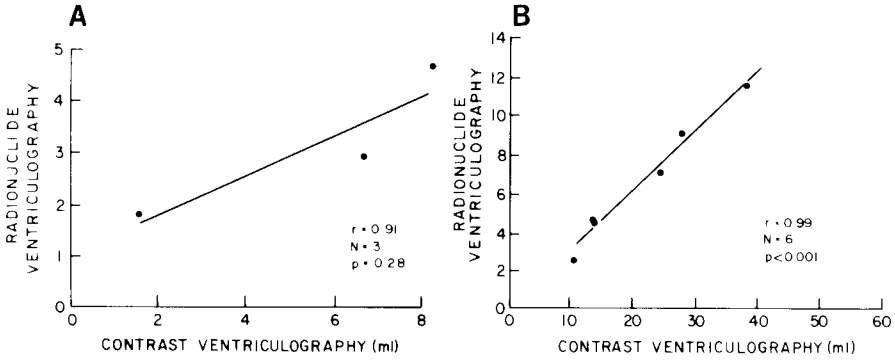
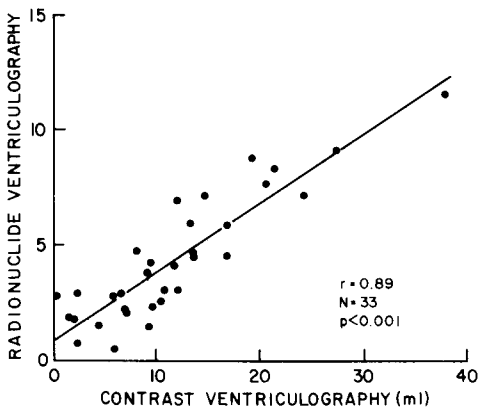


Figure 2. Relation between end-systolic volume changes on radionuclide (units) and contrast (ml) ventriculography. **A**, Dog with smallest volume changes (Dog 3); **B**, dog with largest volume changes (Dog 5). The radionuclide estimates were accurate, even with small changes in volume.

of single beat and gated radionuclide ventriculography in ejection fraction calculations in stable circumstances (31). Thus, the averaging of several cycles for radionuclide ventriculography would be unlikely to cause significant errors. However, multiple factors, such as transient deep inspiration, could affect the left ventricular volume (32) on the single cycles used for contrast ventriculography, and by the experimental design, a single error would be propagated. Thus, in a study with three ventriculograms, a transient change in left ventricular volume during one would affect four of the six values for volume change. With four ventriculograms, one transient change would affect 6 of the 12 values for volume change. Therefore, the close correlations we found in nearly all studies demonstrated the usual stability of the preparation and the accuracy of radionuclide ventriculography for defining volume change. For the entire group of studies there was a good correlation for end-systolic volume changes between radionuclide and contrast ventriculography (r = 0.89) (Fig. 3). This correlation was as good as for the individual animals, because the nature of the calculation of volume change canceled the variable effects of attenuation and background in the individual animals.

Figure 3. Relation between radionuclide and contrast ventriculographic end-systolic volume changes for the group. The radionuclide change (units) correlated well with the contrast ventriculographic change (ml). The correlation was as close as the individual studies, because errors in background subtraction were not a factor in the calculations.



End-systolic pressure-volume relations. In the isolated heart the end-systolic pressure-volume relation is described by the relation: $E_{es} = P_{es}/(V_{es} - V_0)$, where E_{es} is the slope of the relation (elastance), P_{es} and V_{es} are the end-systolic pressure and volume and $V_{0,es}$ is its volume axis intercept (33). We examined the linearity and slope of E_{es} and the values of V_0.

Linearity. The pressure-volume relations were linear using both radionuclide and contrast ventriculography, with r values consistently 0.94 or greater (Table 4), and confirmed prior reports (1–11,13). Our pressure-volume data were generated using phenylephrine-induced blood pressure changes in dogs sedated with morphine and diazepam, and with an atropine infusion to maintain a constant heart rate. Others have reported leftward shifts in the pressure-volume relation during high doses of phenylephrine (34) in the conscious dog, possibly due to beta-adrenergic stimulation. It is possible that sedation of our animals and the atropine accounted for the linearity of our results compared with those in the conscious dog.

Slope. The slope (E_{es}) of the end-systolic pressure-volume relation in our study was similar to that in prior reports in the intact dog (5,6) and in humans (7,10,13,15). The mean slope obtained using the radionuclide method was shallower than that obtained with contrast ventriculography, but the values correlated fairly well (r = 0.81, p = 0.026) despite the limited number of data (n = 7). Because the end-systolic pressures were nearly equal, the cause of the slope difference was probably systematic overestimation of ventricular volume by radionuclide ventriculography or underestimation by contrast ventriculography.

Volume intercept. The calculated volume at zero pressure (V_0) was a negative value in five of the seven dogs using contrast volume estimates and was more negative in all seven dogs using radionuclide estimates (Table 4). The greater negativity resulted from the shallower slopes when using the radionuclide volumes, because V_0 was calculated by a linear equation, rather than measured experimentally.

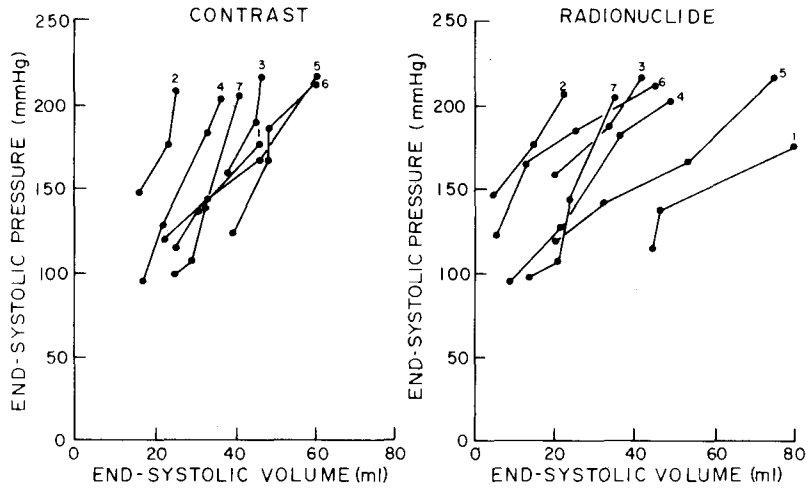


Figure 4. End-systolic pressure-volume relations in seven dogs estimated by contrast and radionuclide ventriculography. Values for each dog are connected **dot to dot** and **small numbers** denote the individual animals. The relations are linear by regression analysis and the slope values correlate (see text for details).

Similar results occur in humans (10,13,15). Thus, ventricular geometry, autonomic innervation and contractility appear to produce conditions that shift V_0 leftward compared with the value in isolated heart. Alternatively, it is possible that the end-systolic pressure-volume relation is nonlinear at low pressures in the intact heart and that V_0 actually is a positive value, but is miscalculated by linear extrapolation. Studies of pressure-volume relations using vena caval occlusion in the concious dog demonstrate nonlinearity at lower pressures (5), but its cause is unclear.

Technical factors affecting volume estimation. Radionuclide estimates of left ventricular volume employ the equation:

$$\text{LVEDV} = \frac{\text{ED counts} - B_D}{(\text{Blood sample counts/ml}) - B} \times A,$$

where LVEDV = left ventricular end-diastolic volume, ED counts = total radioactivity in the left ventricular region of interest at end-diastole, B_D = intrathoracic background radioactivity (counts/pixel) multiplied by the number of left ventricular pixels at end-diastole, A = intrathoracic attenuation and B = background radioactivity in the imaging room. We measured B_D using a standard pericardial region. We measured A by a method that counted the same radioactive source in a catheter in the chest and on its surface. The concept was similar to esophageal transmission measurement (35).

The correlation of radionuclide and contrast volume estimates was excellent for the animals individually ($r = 0.92$ or greater), but when volume data from all dogs were combined, the correlation coefficient decreased (Table 3). This might be due to incorrect estimation of the background or the attenuation. Inspection of the volume equation shows the importance of these two factors. The apparent volume is reduced by background subtraction and is increased by attenuation correction.

Several radionuclide studies have shown 3- to 6-fold underestimation of left ventricular volume after background

Table 4. End-Systolic Pressure-Volume Relations

	Linearity		Slope		V_0	
Dog	RVG	CVG	RVG	CVG	RVG	CVG
1	0.95	0.997	1.53	2.89	−37.5	−15.0
2	0.998	0.95	3.58	6.06	−35.5	−7.6
3	0.995	0.95	2.63	6.17	−39.8	−12.5
4	0.99	0.998	2.89	5.48	−23.9	−0.8
5	0.99	0.99	1.79	2.51	−45.9	−24.3
6	0.94	0.96	2.12	4.08	−59.0	6.5
7	0.97	0.98	5.53	6.69	−0.86	11.3
Mean	0.98	0.97	2.87*	4.84*	−34.8*	−2.5*
SD	0.02	0.02	1.26	1.55	16.7	13.9
SE	0.01	0.01	0.52	0.63	6.3	5.2

*$p < 0.004$ versus corresponding value. V_0 = calculated volume at end-systolic pressure = 0; other abbreviations as in Table 3.

subtraction (17,19,20,23,27–29,36). The cause was probably actual attenuation plus background oversubtraction. The inverse of radioactive attenuation is transmission. Transmission factors for technetium-99m in humans average 0.42 (37), 0.30 (38) and 0.21 (35), values that are roughly similar to our finding of 0.43 in dogs. In this study, after background subtraction the slope (m) of the radionuclide-contrast volume relation was 0.22 (Table 3), similar to the results in clinical studies (17,19,22,23,28,36). By combined background subtraction and attenuation correction the slope of the volume regression was only 0.46, far less than the ideal slope of 1.0, but by attenuation correction alone the regression slope was 1.06. Thus, oversubtraction of the background radioactivity was likely in this study, and possibly in several clinical studies, based on the similarity of our data to their results.

Recent reports emphasized attenuation correction to improve radionuclide volume estimates (19–21,35,37,39); however, only Seiderer et al. (19) analyzed the effects of background subtraction. Their results with and without uniform background subtraction are highly similar to ours, and the effects of attenuation are directionally similar. Cardiac background activity has been directly measured in dogs given thallium-201 and imaged before and after excising the heart (40). There was an average 85% overestimation using the standard pericardial region as the background. Scatter of radioactivity (cross-talk) from the heart and adjacent structures was the likely cause. Applying this additional background correction and our measured attenuation factor (2.3) to our results yielded a slope of 0.94.

Correction for background and for attenuation might be more useful than background subtraction alone for estimating left ventricular volume, if warranted by the results. Although attenuation correction improved the radionuclide-contrast volume correlation compared with background subtraction alone, there was no improvement using combined background and attenuation correction. In addition, the correlations for volume changes and the pressure-volume relation were not improved by any of these maneuvers. Thus, for simplicity, we employed background subtraction and a regression equation to correct for oversubtraction. The results for volume changes and the pressure-volume relations correlated well because any errors were likely to be constant in each animal. Recently, Starling et al. (20) showed improved r values and tighter 95% confidence limits for volume estimation in humans by background subtraction and geometric attenuation correction. Further work is necessary to establish optimal methods and to evaluate whether they translate into improved results in physiologic testing.

Limitations of the study. These data were obtained in dogs, and with a higher dose of technetium pertechnetate than used clinically. It is possible that the thinner chest wall and greater radioactivity in the dog may improve the results beyond those obtainable clinically. Thus, the results might be applicable only to similar canine models. However, some confidence about clinical applicability is permissible, because the canine images were not of observably better quality than the clinical images. Also, we found no significant differences between clinical and canine images in radioactivity per pixel using the same camera-computer system.

Conclusions. This study demonstrated that estimates of systolic volume changes using radionuclide ventriculography were accurate, even though these changes averaged only 11 ml and were often very small. The sources of some of the errors in radionuclide volume estimates were analyzed and understood. The results established that radionuclide ventriculography was a reliable method for determining the left ventricular volume change in this model and that end-systolic pressure-volume estimates using radionuclide ventriculography are likely to be accurate.

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